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| 10/561,985 | 01/13/2006 | Philip Alfred Ropp | 2003.795US | 1515 |
| 67706 7590 10/19/2009 ORGANON USA, INC. c/o Schering-Plough Corporation 2000 Galloping Hill Road Mail Stop: K-6-1, 1990 Kenilworth, NJ 07033 | | | | |
| | | | EXAMINER DEVI, SARVAMANGALA / N | |
| | | | ART UNIT 1645 | PAPER NUMBER |
| | | | NOTIFICATION DATE 10/19/2009 | DELIVERY MODE ELECTRONIC |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/561,985

Applicant(s)

ROPP ET AL.

Examiner

S. Devi, Ph.D.

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07/15/09.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

- 1) Acknowledgment is made of Applicants' amendment filed 07/15/09 and 03/23/09 in response to the non-final Office Action mailed 09/23/08.

Status of Claims

- 2) Claim 18 has been canceled via the amendment filed 03/23/09.
Claims 1, 7 and 17 have been amended via the amendment filed 03/23/09.
Claims 1-17 are pending and are under examination.

Prior Citation of Title 35 Sections

- 3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

- 4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Maintained

- 5) The objection to the specification made in paragraph 6 of the Office Action mailed 03/23/09 is maintained for the reasons set forth therein and herein below.

It is noted that Applicants have amended the specification to correct most of the trademark recitations. However, the specification still contains one or more trademark recitations that are not capitalized. For example, see the paragraph starting at line 11 of page 21 and the paragraph starting at line 17 of page 4 of the specification for 'Zwittergent 3-14'. It is once again suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

Objection(s) Withdrawn

- 6) The objection to claim 1 made in paragraph 11 of the Office Action mailed 03/23/09 is withdrawn in light of Applicants' amendment to the claim.

Rejection(s) Moot

7) The rejection of claim 18 made in paragraph 10 of the Office Action mailed 03/23/09 under 35 U.S.C. § 102(e)(2) as being anticipated by Hauser *et al.* (US 6,966,992) in light of Petsch *et al.* (*J. Biotechnol.* 76: 97-119, 2000 – Applicants' IDS), is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 18 made in paragraph 8 of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

9) The rejection of claim 1 made in paragraph 8(d) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

10) The rejection of claim 1 made in paragraph 8(e) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

11) The rejection of claim 17 made in paragraph 8(f) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claim 7 made in paragraph 8(h) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

13) The rejection of claims 1-3, 5, 6, 8-10, 11, 14, 15 and 17 made in paragraph 10 of the Office Action mailed 03/23/09 under 35 U.S.C. § 102(e)(2) as being anticipated by Hauser *et al.* (US 6,966,992) in light of Petsch *et al.* (*J. Biotechnol.* 76: 97-119, 2000 – Applicants' IDS), is currently withdrawn in light of the indeterminate and internally inconsistent scope of the claims and the base claims. See 35 U.S.C. § 112, second paragraph rejections. The relevance of the disclosure of Hauser *et al.* to the instant claims would be determined once Applicants address the internally inconsistent scope of the claims under 35 U.S.C. § 112, second paragraph.

Rejection(s) Maintained

14) The rejection of claims 1 and 17 made in paragraph 8(a) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and in the paragraph immediately below.

15) The rejection of claim 14 made in paragraph 8(b) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and herein below.

Applicants submit that the term 'portion of the LPS/protein/endotoxin' refers, not to a part of the structure of the LPS-protein or endotoxin but rather refers to a part of the entire amount (a portion) of the LPS, protein, or endotoxin present. Applicants state that this is also made clear to the skilled artisan reading the specification in the recitations on page 7, line 13 to page 8, line 2 and page 8, lines 7-18 of the specification. Applicants state that these paragraphs clearly discuss a portion of the LPS/protein/endotoxin as a relative amount of the total amount of the LPS/protein/endotoxin.

Applicants' arguments have been carefully considered, but are not persuasive. The parts of the specification identified by Applicants describe that greater than 50%, 75%, 80%, 85%, 90%, 95%, 97%, 99% and 99.9% of the LPS is separated from the LPS-protein complex. Similarly, specific percentage(s) of the protein eluted is described herein. The claims remain indefinite and confusing particularly in view of Applicants' assertion that endotoxin and LPS represent different toxins and that LPS is a subset of endotoxins (see page 14 of Applicants/ amendment/response filed 07/15/09) and that the endotoxic component of LPS is the lipid A 'portion' (see second full paragraph on page 16 of Applicants/ amendment/response filed 07/15/09). Line 1 of the claims recites that the process is for 'removing an endotoxin', i.e., lipid A 'portion', or 'a portion of the LPS' as recited in line 5 of claim 1 and line 6 of claim 17. Thus, by Applicants' own acknowledgment, 'a portion of the LPS' does not necessarily mean a relative amount of the total amount. Does the limitation 'a portion of the endotoxin' as recited in line 3 of claim 14 mean or encompass 'a portion of lipid A'? The rejections stand.

16) The rejection of claim 1 made in paragraph 8(c) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and in the paragraph immediately below.

17) The rejection of claim 7 made in paragraph 8(g) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and in the paragraph below.

Applicants submit that the term 'endotoxin' refers to a broader group of bacterial toxins and that 'Lipopolysaccharides' constitute a subset thereof. Applicants assert that the skilled artisan would understand that the terms 'the LPS' and 'endotoxin' represent 'different' toxins, wherein LPS represents a subset of endotoxins.

Applicants' arguments have been carefully considered, but are not persuasive. As recited currently, the 'other endotoxin' recited in claim 7 is different from 'an endotoxin' recited in the base claim 1. The two are not of the same scope. With the Applicants' statement that 'LPS' and 'endotoxin' represent different toxins and the LPS is a subset of endotoxins, the scope of the claims is indeterminate, because what is being removed in the claimed process as recited in claim 1 is 'an endotoxin' of broader scope, whereas what is separated from the complex after the washing step is 'a portion of the LPS', i.e., the lipid A component of LPS, the LPS being of narrower scope, i.e., a subset of endotoxin. It is unclear how separation of 'at least a portion of the LPS', i.e., the lipid A component of LPS, amounts to the removal of the whole 'endotoxin' from recombinantly produced proteins. The scope of the claims is internally inconsistent. The rejections stand.

18) The rejection of claim 11 made in paragraph 8(i) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and herein below.

Applicants submit that the claimed processes relate to separating (eluting) either the LPS, endotoxin, or protein from a (chromatographic) resin. Applicants state that in the art of removing material of biological origin, either LPS, endotoxin, or protein, from a chromatographic resin, particularly in obtaining recombinant proteins from a bacterial expression system, the skilled artisan would immediately understand the meaning of the term 'high salt environment' in this context.

Applicants' arguments have been carefully considered, but are not persuasive. As set forth previously, the term 'high' is a relative term which is not specifically defined by the claim,

and the specification does not provide a standard for ascertaining the requisite degree. Without a description of 'high' in comparison with what, one of skill in the art cannot understand the scope and the meaning of the limitation: 'high salt environment'. The rejection stands.

19) The rejection of claim 13 made in paragraph 8(j) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and in the paragraph immediately below.

20) The rejection of claims 8 and 17 made in paragraph 8(k) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and herein below.

Applicants submit that the claimed processes relate to separating (eluting) either the LPS, endotoxin, or protein from a (chromatographic) resin. Applicants state that in the art of removing material of biological origin (either LPS, endotoxin, or protein) from a chromatographic resin, in particularly in obtaining (recombinant) proteins from a bacterial expression system, the skilled artisan would immediately understand the meaning of the terms 'changing pH' or 'a change in pH or conductivity' in this context as is also made clear in the specification on page 8, lines 3-6. With this, Applicants conclude that claims 8, 13, and 17 clearly define the claimed subject matter.

Applicants' arguments have been carefully considered, but are not persuasive. The chromatographic resin recited in the claims has several components, including the resin, alkanediol used to wash the resin to separate (elute) a portion the LPS, the protein, and perhaps a medium in which the resin is maintained. A change in conductivity or pH of which of these elements(s), or of the whole flow is encompassed in the elution step is not clear. The rejections stand.

21) The rejection of claims of 2-13, 15 and 16 made in paragraph 8(l) of the Office Action mailed 03/23/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for the reasons set for the therein.

New rejection(s) Necessitated by Applicants' Amendment

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

22) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

23) Claims 1-13 and 17 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 1 and 17, as amended, are indefinite and confusing in the limitations: 'recombinantly produced proteins' and 'a protein' (see lines 1-3), because the limitation 'a protein' is of broader scope than the limitation 'recombinantly produced proteins' because it encompasses non-recombinant proteins. The two limitations are of different scope. Is what is eluted at the end of the claimed process a non-recombinant protein? Is 'the protein' in the last part of claim 17 a non-recombinant protein impurity?

(b) Claim 17, as amended, is further confusing and indefinite in the limitation 'affixing the LPS ... to an anion ... resin' and 'a portion of the LPS is separated from the complex'. Is 'a portion of the LPS separated' a portion of the LPS, i.e., the lipid A portion, affixed to the anion resin? Is what is being removed via the claimed process the whole endotoxin, or a subset of endotoxin, i.e., LPS, or 'at least a portion of the LPS', i.e., the lipid A component of LPS? Clarification is requested.

(c) Claims 2-13, which depend directly or indirectly from claim 1, are also rejected as being indefinite due to the indefiniteness identified above in the base claim.

Remarks

24) Claims 1-17 stand rejected.

25) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

26) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

27) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.Mov>. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

28) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

October, 2009